

Claims

- 5 1. Osteoinductive material comprising a matrix material and, adsorbed on inner and/or outer surfaces of this matrix material morphogenetic, protein(s), wherein the osteoinductive material is obtainable by contacting the matrix material and the morphogenetic protein(s) under suitable conditions to keep the protein stable and dissolved in a solution, thereby allowing that the matrix material becomes evenly
10 coated with the morphogenetic protein(s).
2. Osteoinductive material according to claim 1, wherein the morphogenetic protein contains at least a 7 cysteine region characteristic for TGF- β superfamily proteins.
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3. Osteoinductive material according to claim 1 or 2, wherein the morphogenetic protein is a mature protein or a biologically active part or variant thereof.
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4. Osteoinductive material according to anyone of claims 1 to 3, wherein the morphogenetic protein belongs to the TGF- β -, BMP-, GDF-, activin- or GDNF-family.
- 25 5. Osteoinductive material according to anyone of claims 1 to 4, wherein the morphogenetic protein is a dimeric protein.
6. Osteoinductive material according to anyone of claims 1 to 5, wherein the morphogenetic protein is BMP2, BMP7, BMP12, BMP13, MP52 (GDF5) or a biologically active part or variant thereof.
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7. Osteoinductive material according to anyone of claims 1 to 4, wherein the morphogenetic protein is a protein lacking the cysteine residue which is

- 36 -

responsible for dimer formation in the respective naturally occurring proteins.

- 5 8. Osteoinductive material according to anyone of claims 1 to 4 and 7, wherein the morphogenetic protein contains a consensus sequence according to

Formula I: $C(Y)_{25-29}CYYYC(Y)_{25-35}XC(Y)_{27-34}CYC$ or

Formula II: $C(Y)_{28}CYYYC(Y)_{30-32}XC(Y)_{31}CYC$,

- 10 wherein C denotes cysteine, Y denotes any amino acid and X denotes any amino acid except cysteine.

9. Osteoinductive material according to anyone of claims 1 to 4, 7 and 8, wherein the protein is a monomeric form of MP52.

- 15 10. Osteoinductive material according to anyone of claim 9, wherein the protein is MP52-Ala83 or a biologically active part or variant thereof.

11. Osteoinductive material according to anyone of the preceding claims, wherein the matrix material is a biocompatible material.

- 20 12. Osteoinductive material according to anyone of the preceding claims, wherein the matrix material is a natural material, a modified natural material or a synthetic material.

- 25 13. Osteoinductive material according to anyone of the preceding claims, wherein the matrix material is a porous material.

- 30 14. Osteoinductive material according to anyone of the preceding claims, wherein the matrix material comprises at least one of the following substances: a) collagen, b) $Ca(OH)_2$, c) polylactide or polylactide derivatives, d) hyaluronic acid, e) polyoxyethylene polyoxypropylene copolymers f) calcium phosphate, g) a combination of hydroxy apatite and collagen h) a combination of polyglycolic acid and polylactic acid or

- 37 -

polylactid derivatives.

- 5 15. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating has a ionic concentration of 150 mmol/l or less, 100 mmol/l or less, 80 mmol/l or less, 40 mmol/l or less, 20 mmol/l or less, 10 mmol/l or less, or 5 mmol/l.
- 10 16. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating further comprises saccharides.
- 15 17. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating further comprises alcohols or other organic solvents.
18. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating further comprises soaps or syndets.
- 20 19. Osteoinductive material according to any of the preceding claims, wherein the morphogenetic protein(s) is covalently or noncovalently linked to polyethylene glycols.
- 25 20. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating is capable of maintaining a pH below 5.2.
- 30 21. Osteoinductive material according to claim 20, wherein the buffer or solvent used for coating contains HCl or sodium acetate.
22. Osteoinductive material according to anyone of the preceding claims, wherein the buffer or solvent used for coating is capable of maintaining a pH above 9.5.

- 38 -

23. Osteoinductive material according to claim 22, wherein the buffer or solvent used for coating contains NaOH or sodium carbonate/sodium bicarbonate.

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24. Process for the production of an osteoinductive material according to claims 1 to 21, said process comprising contacting a matrix material with a solution of at least one morphogenetic protein characterized in that substances contained in said solution are selected to enable adjustment of the pH of the solution to below 5.2 even when in contact with the matrix material.

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25. Process for the production of an osteoinductive material according to claims 1 to 19, 22 and 23, said process comprising contacting a matrix material with a solution of a morphogenetic protein characterized in that substances contained in said solution are selected to enable adjustment of the pH of the solution to above 9.5 even when in contact with the matrix material.

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26. Use of an osteoinductive material according to claims 1 to 23 for indications in which monomeric or dimeric morphogenetic proteins have been proven to be useful.

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27. Use according to claim 26, wherein the osteoinductive material is used for preventing, alleviating or treating symptoms or conditions of diseases or abnormal conditions of cartilage, bone, connective tissue including tendon and/or ligament, periodontal or dental tissue, neural tissue, tissue of the sensory system, liver, pancreas, cardiac, blood vessels, renal, uterine and thyroid tissue, skin, mucous membranes, endothelium, or epithelium.

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28. Use according to claim 26 or 27, for promotion or induction of nerve growth, tissue repair and regeneration, angiogenesis, wound healing

- 39 -

including ulcers, burns, injuries or skin grafts, induction of proliferation of progenitor cells or bone marrow cells, for regeneration of functional attachment between connective tissue and bone, cartilage repair, treatment of osteoporosis or osteoarthritis, to correct non-union fractures, acquired or congenital craniofacial, skeletal or dental abnormalities, for non-skeletal tissue replacement in plastic or reconstructive surgery.

29. Use according to anyone of claims 26-28, wherein the disease or abnormal condition is caused by ischemic or traumatic injury, degenerative disease, cardiomyopathies, atherothrombotic or cardioembolic strokes, ulceration, cirrhosis, emphysema, cell senescence or quiescence.